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Demographics and inflammatory features correlate in lumbar disc hernia

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Abstract

Aim: In patients with lumbar disc hernia, the demographic and inflammatory factors that are mutually associated with each other and radicular pain are not entirely clear. This study aimed to determine these correlations.

Material and Methods: This retrospective investigation evaluated 124 lumbar disc hernia patients selected according to detailed inclusion and exclusion criteria to minimize bias factors. The study determined the patient's demographic and clinical features, comorbid diseases, pain intensity, disc hernia side and levels, extent of paresis, and inflammatory indices (neutrophil-to-lymphocyte and platelet-to-lymphocyte ratio). Pain intensity was assessed with Visual Analogue Scale (VAS) scores. Inflammation indices are calculated from blood counts. NCSS (Number Cruncher Statistical System, 2020, USA) software was utilized for statistical analysis.

Results: Patient's age, extent of paresis, and disc hernia side correlated with pain intensities. Patients with disc hernias at the L1-L2 and L5-S1 levels had shorter preoperative pain duration than the cohort's median pain duration, while the reverse was true for L2-L3 and L4-L5 level disc hernias. Twelve patients (9.7%) had comorbid diabetes, demonstrating a lower reduction of immediate postoperative pain. There was a slight negative correlation between the neutrophil-to-lymphocyte ratio and the preoperative pain duration.

Discussion: This current study provides additional insights regarding demographics, anatomy, and inflammatory components of disc hernia.

Keywords

Lumbar Disc Hernia, Microdiscectomy, Demographics, Inflammation

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Introduction

Lumbosacral disc hernia is the most common cause of lower back and leg pain. Lumbosacral radiculopathy is an impairment of nerve roots causing any blend of motor paresis, sensory disturbance, and pain depending on the compression degree on nerve roots [1]. The most common causes of lumbar radiculopathy are disc hernia and spondylosis. Less-defined aspects of disc hernia exist, including inflammation, comorbid diseases, and their association with pain. Also, determining the mutual interactions of these factors with hernia anatomy and the extent of paresis would provide novel insights into the disc hernia. These factors are overlooked in the daily practice of surgeons performing spine surgery. However, despite successful surgery, a recurrence of patient's pain complaints in the absence or presence of newly protruded discs is encountered in several cases. Hence, in this retrospective study, we investigated these parameters and their associations in a patient cohort (n=124) with single-level lumbar disc hernia treated with microdiscectomy.

Material and Methods

Study Design and Treatment

This clinical study complied with the Helsinki Declaration's rules and the latest amendments. All participating patients gave consent forms after obtaining information about the study. The local ethics committee permitted the study (Decision Number: 74, 2023-01-05). The study involved 124 participants, 68 men and 56 women, operated at the same institution, Memorial Bahçelievler Hospital (Istanbul, Turkey). Patients were between 19 and 78 years old and had radiological features of single-level lumbar disc hernias compatible with lumbar radicular pain. In all patients, radicular pain or neurogenic claudication accompanied spinal stenosis on imaging. The main criteria to define the surgical timing were either the patient's declaration that the pain is unbearable or the extent of motor paresis, which may cause irreversible neurological damage if left untreated. The exclusion criteria were prior fractures in the hernia region, primary and metastatic tumors, degenerative vertebral disease, and spinal malformations. The patients with previous lumbar disc operations or other pain-related neural, osteological, and muscular diseases were also excluded. The diabetic patients in the study cohort were confirmed not to suffer from diabetic neuropathy by a consultant neurologist. All patients underwent single- level simple lumbar microdiscectomy with partial hemilaminectomy + flavectomy and foraminotomy under the surgical microscope.

Data Collection

The assessed information included demographic data (gender, age, comorbid diseases), herniation level and sides, intensity and duration of preoperative pain, postoperative pain alleviation, paresis, neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR). Visual Analogue Scale (VAS) was used to evaluate pain intensity at preoperative, immediate postoperative, and in the 3rd and 6th months of the postoperative period. Clinical examinations determined the extent of paresis semi-quantitatively using a scale between 0 to 5, reflecting motor deficit and loss of muscle strength from absent to complete. The current study analyzed mutual associations of all the assessed parameters and compared inflammatory and demographic features stratified according to the median duration of preoperative pain, which was 14.5 days in the cohort. Lastly, the study revealed NLR and PLR associations with demographic features, extent of paresis, and pain intensity.

Statistics

NCSS (Number Cruncher Statistical System, 2007, Utah, USA) was utilized for statistics. Student's –T-test and the Mann-Whitney U test were used to compare quantitative variables with normal and non-normal distribution, respectively. Fisher's Exact and Fisher-Freeman-Halton tests were used for chi-square analysis. The Kruskal-Wallis test was utilized to determine the significance of the difference between the means of three or more groups in non-normally distributed groups. Lastly, Spearman's correlation analysis was performed to evaluate the relationships between quantitative variables. Statistical significance was accepted as $p<0.05$.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

Demographic, Anatomical and Pain Features

The total number of participants was 124 (68 males, 56 females). The median age of patients was 45 (19-78). While the preoperative pain of 63 patients (50.8%) lasted for 14 days or less, it lasted for 15 days or more in 61 patients (49.2%). The median and mean pain durations were 14.5 (1-365) and 46,62±12,71 days, respectively. Fifty-two patients (41.9%) had right-sided, and 72 patients (58.1%) had left-sided disc hernia. The number and percentages of patients with diabetes mellitus, coronary disease, thyroid diseases, and other different pathologies were 12 (9.7%), 5 (4.0%), 4 (3.2%), and 13 (10.5%), respectively. Two (1.6%), 3 (2.4%), 9 (7.3%), 67 (54.0%), and 43 (34.7%) patients had disc hernias at the levels L1-L2, L2-L3, L3-L4, L4-L5, and L5-S1, respectively. All patients had pain and paresis at the ipsilateral side of the disc hernia. Thirty-nine patients (31.5%) had no paresis, while the remaining 85 (68.5%) had paresis at different degrees. Forty-one (33.1%), 27 (21.8%), 10 (8.1%), and 7 (5.6%) patients had an extent of paresis (motor deficit) defined as 1, 2, 3, 4, respectively. There were no patients with complete paresis. The mean preoperative VAS score of the patients was 9.10±0.69. These values reduced to 1.53±1.07, 1.35±1.12, and 1.24±1.16 at the immediate postoperative, 3rd and 6th postoperative months, respectively. All these pain reductions were statistically significant ($p<0.0001$) at all time points. Preoperative pain in patients without paresis was significantly higher than in those with 1 ($p=0.036$). Postoperative 6th month VAS pain values in those without paresis were significantly higher than in those with 3 ($p=0.017$). Patients younger than the median age of the patient cohort tended to have higher preoperative pain than patients older than the median age ($p=0.051$). Patients with left-sided disc hernias had higher preoperative pain intensity ($p=0.028$).

Patient's Features According to Preoperative Pain

Table 1 summarizes the characteristics of disc hernia patients stratified according to the preoperative pain duration. The percentages of patients both without paresis (39.7%) and

Table 1. NLR and PLR values, hernia levels and extent of paresis evaluated according to the preoperative pain duration.

Patients Features	Duration ≤14 days (n=63)	Duration ≥ 15 days (n=61)	P- value
Hernia Level; n(%)			
L1-L2	2 (3,2)	0 (0)	[a]0,007*
L2-L3	0 (0)	3 (4,9)	
L3-L4	5 (7,9)	4 (6,6)	
L4-L5	27 (42,9)	40 (65,6)	
L5-S1	29 (46)	14 (23)	
Extent of Paresis; n(%)			
0	25 (39,7)	14 (23,0)	[a]0,011*
1	13 (20,6)	28 (45,9)	
2	13 (20,6)	14 (23,0)	
3	6 (9,5)	6 (6,6)	
4	6 (9,5)	1 (1,6)	
NLR			
Mean±Std	3,42±2,08	2,86±1,37	[b]0,034*
Median (Min-Max)	3,05(1,1-16)	1,63 (0,9-8,5)	
PLR			
Mean±Std	121,76±48,06	126,13±35,87	[b]0,281
Median (Min-Max)	113,2 (45,1-294,9)	119,8 (66,2-249,5)	

[a]Fisher- Freeman- Halton Test, [b]Mann-Whitney U Test

level 4 paresis (9.5%) were significantly higher in patients with shorter duration (≤14 days) of pain. NLR values differed among different pain durations; those with shorter preoperative pain duration had higher NLR levels (p=0.034). A lack of significant difference was noted for PLR when stratified according to preoperative pain duration (p=0.281).

NLR and PLR Correlations With Clinical Features

NLR values of the cases ranged from 0.9 to 16 with a median of 3.15±1.79. The PLR values of the cases ranged from 15.1 to 294.9 with a median of 115.7. Table 2 demonstrates the associations of NLR and PLR values with pain intensity. NLR and PLR values did not correlate with preoperative and postoperative pain except for a tendency of negative correlation between NLR and immediate postoperative pain (r=-0.183, p=0.051). A slight statistical correlation also existed between the pain duration and NLR values (r=-0.191, p=0.042; not shown in Table). Table 3 demonstrates comparisons of NLR and PLR values stratified according to demographics, hernia anatomy, and the extent of paresis.

Effects of Diabetes

Diabetes was present in 9.7% of the study cohort. Preoperative VAS scores did not differ between patients with or without diabetes (p>0.05), but the immediate postoperative pain scores were higher in diabetic patients (p=0.002). The change in VAS scores in the immediate postoperative period also highly differed according to the presence of diabetes (p=0.001).

Table 2. NLR and PLR comparisons with pain intensity at different periods.

VAS Score			Pre	Imm	Post 3rd	Post 6th	Change Pre vs Imm	Pre vs Post 3rd	Pre vs Post 6th
NLR	p	r	-0,086	-0,183	-0,023	-0,076	0,116	-0,026	0,029
			0,364	0,051	0,804	0,444	0,218	0,786	0,773
PLR	p	r	-0,033	-0,018	0,049	-0,05	-0,013	-0,073	0,071
			0,721	0,845	0,605	0,608	0,887	0,437	0,467

r: Spearman's Correlation Coefficient. p: Significance value. Pre: Preoperative evaluation. Post 3rd: Postoperative 3rd month evaluation. Post 6th: Postoperative 6th month evaluation. Imm: Immediate postoperative evaluation. vs: Versus

Table 3. NLR and PLR value comparisons with patient demographic features and paresis.

		NLR Mean+SD	NLR Median (Min-Max)	p	PLR Mean+SD	PLR Median (Min-Max)	p
Age	Age <45	3,13±2,10	2,8(1,1-16)	[b]0,325	126,07±48,11	114,8(45,2-294,9)	[b]0,784
	Age ≥ 46	3,18±1,41	3,1(0,9-8,5)		121,43±35,52	116,5(55,9-249,5)	
Gender	Male	3,31±2,17	2,9(1,1-16)	[b]0,831	119,11±44,78	110,7(45,2-294,9)	[b]0,069
	Female	2,98±1,19	2,9 (0,9-6,3)		129,34±39,40	120,9(48-225,4)	
Diabetes	Absent	3,23±1,28	3,1 (0,9-5,9)	[b]0,517	121,62±35,54	117,4(70-213,5)	[b]0,387
	Present	2,99±1,15	2,9 (1,1-5,5)		111,96±32,52	109,7(66,7-181)	
Level	L4-L5	3,12±1,29	2,9 (1,1-8,5)	[b]0,740	122,07±39,66	116,1(45,2-249,5)	[b]0,851
	L5-S1	3,25±2,37	2,8 (1,1-16)		122,80±43,55	112,3(48-294,9)	
Side	Right	3,29±2,31	2,9 (1,1-16)	[b]0,901	132,47±44,45	125,1(59,9-294,9)	[b]0,051
	Left	3,06±1,34	2,9 (0,9-8,5)		118,02±40,39	109,9(45,2-249,5)	
Paresis	0	3,02±2,56	2,5 (0,9-16)	[c]0,193	122,66±49,71	110,8(45,2-294,9)	[c]0,719
	1	3,06±1,03	2,9 (1,1-5,9)		122,37±30,65	113,1(78,1-224,1)	
	2	3,13±1,21	3 (1,1-6)		123,50±36,95	119,8(55,9-217,6)	
	3	4,08±2,38	3,4 (1,7-8,5)		148,08±67,77	131,1(48-249,5)	
	4	3,24±0,51	3,2 (2,4-4)		108,64±31,22	116,5(59,9-147,9)	

[b]Mann-Whitney U Test; [c]Kruskal-Wallis Test

Discussion

Demographics, paresis and disc hernia level

The lower preoperative pain in older patients is likely attributable to the aging-associated chronic disc degeneration and subsequent increase in pain thresholds. Lower preoperative pain observed in patients with paresis may be associated with the denervation, where intense damage on nerve root fibers transmitting pain signals may alleviate pain. Postoperative 6th month pain in patients without paresis was higher than in those with level 3 paresis. Pain recurrence at a relatively later period may be associated more with inflammation, as reduced long-term pain control after disc hernia surgery is associated with lower circulating cortisol and higher inflammatory IL-6 [2]. The extent of paresis statistically differed according to the preoperative pain. Peculiarly, the percentage of patients without paresis (39.7%) and with level 4 paresis (9.5%) was higher among patients with shorter preoperative pain duration. This feature may be associated with diverging patient types requiring immediate surgery: patients with no motor deficit but not tolerating pain and patients who may partially cope with pain but present with significant motor deficits. L1-2 and L5-S1 level disc hernia cases accumulated more in the group with a shorter duration of preoperative pain, while the reverse was true for L2-3 and L4-5 disc hernia cases. This finding may be incidental due to the low number of patients or the mid-lumbar region hernias causing more intense pain and earlier surgeries. The patients with right-sided hernia had higher preoperative pain, but postoperative pain did not correlate with the lesion side. This observation is consistent with findings suggesting that right-sided disc hernias were usually more extensive in patients with radicular pain [3].

Diabetes in disc hernia patients

In this cohort, a notable proportion of cases had diabetes mellitus, which showed a reduced decline in the VAS scores during the immediate postoperative period. The association of diabetes with disc hernia is explicable with inflammatory cytokines, subchondral vertebral endplate microangiopathy, senescence, apoptosis, autophagia of intradiscal chondrocytes, and advanced glycation end products (AGEs) [4]. In disc hernia surgery, higher pain positively correlates with circulating IL-6, an inflammatory cytokine related to diabetic hyperalgesia [5]. Thus, diabetes-induced inflammation may have contributed to disc disease and lesser pain alleviation.

Blood inflammatory indices

The extruded nucleus pulposus attracts leukocytes and induces neural root inflammation [1]. In rats, depletion of leukocytes with nitrogen mustard prevented nucleus pulposus-induced hyperalgesia [6]. The neutrophil-to-Lymphocyte Ratio (NLR) is an inflammatory marker obtainable from blood counts. In 20 patients receiving lumbar disc hernia surgery, a positive correlation existed between the NLR values and VAS scores measured at the preoperative and postoperative periods [7]. A study examined lumbar magnetic resonance imaging (MRI) features, NLR values, and usage of nicotine products in 87 lumbar disc hernia patients [8]. Mutual positive correlations existed between the level of nicotine consumption, inflammation, and the extent of disc hernia [8]. An analysis of 126 patients with neck pain revealed that MRI-demonstrated cervical hernia patients had higher NLR and CRP levels than healthy controls and those with pain without MRI pathology [9]. Another study defined inflammatory indices MI-1 and MI-2, by multiplying PLR and NLR values with CRP values, respectively, and found that MI-1 and MI-2 correlated positively with lumbar pain [10]. This current study's results differ from those of previous studies since NLR values were higher in patients with shorter preoperative pain duration. This feature may be associated with a higher inflammatory state in these patients. NLR values and immediate postoperative pain scores had a slight negative correlation, likely due to higher surgical benefits for patients with increased inflammation who achieved pain relief after the excision of the inflammatory disc material.

The current study has limitations as it is retrospective, and the VAS method is subjective. The data regarding the pain duration by disc level are limited since the patient's numbers were low except for L4/5 and L5/S1 hernias. The association of diabetes with disc disease needs to be assessed in larger cohorts as the data pertains to a small number of patients. Nonetheless, the current study also has strengths. Detailed inclusion and exclusion criteria allowed reliable analyses in a homogenous cohort. All the patients were treated in the same institution, eliminating heterogeneities regarding surgery decisions and timing criteria, VAS assessments, and physical examination.

Conclusion

The pain and paresis in disc hernia occur due to a blend of anatomical and inflammatory factors, which may differentially contribute to disease among different age groups. More extensive studies with prolonged assessments of blood indices are necessary to prove the proposals of this study. Also, the role of diabetes in hernia pathogenesis needs further investigation. A better understanding of the contribution degree of anatomical characteristics and inflammation in disc hernia will help to achieve better patient management.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of interest

The authors declare no conflict of interest.

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